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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,604	08/02/2001	Nagaraja K.R. Rao	4172-36	7723

22442 7590 04/07/2004

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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/922,604	RAO ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' species election is acknowledged (the compound in which R^1 is the side chain of aspartic acid in the final product, and R^2 is methyl).

35 U.S.C. §101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture or composition of matter or any new and useful improvement therof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1 and 11 recite that unwanted side reactions can be "prevented". The term "prevention" implies that in fully 100% of all reaction attempts, not a single molecule of the "second amino acid derivative" or the dipeptide will undergo any reaction other than those specifically indicated in the claim. However, the reality in organic synthesis is that impurities are nearly always formed whether protecting groups are present or not. Certainly, if one were to carry out a series of 1000 reactions under a variety of conditions, one would expect that at least in one of those reactions, 0.1% of the protecting groups on the amino or carboxyl substituent would come off, and an "unwanted side reaction" would occur. Nor are the "side reactions" limited to substitution on the amino or carboxyl groups. For example, one potentially "unwanted" side reaction is racemization, which often accompanies diketopiperazine

formation. If the reaction were carried out 100 times, and if in one of those reactions, 0.1% of the hydrogen atoms bonded to the carbon bearing R^2 were transiently removed and subsequently replaced, the result would be racemization, and the fact of this would be proof that any and all "unwanted side reactions" had not in fact been prevented.

It is suggested that the term "prevented" be removed from the claims, and that another term be used which "leaves the door open" for an occasional (if very rare) side reaction to occur.

Claims 1 and 11 are rejected under 35 USC §101 because the claimed invention is not supported by a well established utility.

Claims 1 and 11 are also rejected under 35 USC §112 first paragraph. Specifically, since the claimed invention is not supported by a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The cited claims require removal of the R^5 group by hydrogenation. While it may be clear how this should be done in the case of R^5 representing benzyl, it is not clear how this can be done in the case of R^5 being alkyl, or R^5 being alkylaryl (other than benzyl).

The specification provides no guidance in this regard, and moreover, this assertion runs contrary to what is known in the peptide synthesis art and organic synthetic chemistry in general.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

"Undue experimentation" would be required to remove R^5 groups other than benzyl.

✧

Claims 1-20 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 1 recites (page 18, line 4) that certain side reactions may be "unwanted". The term "unwanted" suggests an emotional component to the decision-making process, and certainly the decision as to what may be wanted or unwanted is highly subjective. Applicants cannot presume to know what a synthetic organic chemist might want or not want at some point in the future. Accordingly, the claim is rendered indefinite.

- In claim 1, a formula 2 is referred to, but no structure of formula 2 is specifically identified. In addition, reference to a formula 2 tends to suggest that a "formula 1" might be present, but no such formula is indicated in claim 1.

✧

The following is a quotation of the appropriate paragraphs of 35 U.S.C §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 8 and 9 are rejected under 35 U.S.C. §102(b) as being anticipated by Milstein

(WO 96/10396) or Milstein (WO 96/09813)

Milstein discloses (page 13 of 10396; page 16 of 09813) preparing the diketopiperazine of glutamic acid by first condensing one molecule of glutamic acid with another (forming a dipeptide), then forming a diketopiperazine from that, yielding diketopiperazine glutamic acid dibenzyl ester, which was subsequently treated with hydrogen/Pd/C to remove the benzyl groups.

Thus, the claims are anticipated.

✧

The following is a quotation of 35 USC. §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 11, 15, 16 are rejected under 35 U.S.C. §103 as being unpatentable over Smith (*Bioorg Med Chem Lett* 8, 2369, 1998).

Smith discloses (page 2370) a process of preparing diketopiperazines on a solid phase support by a process comprising the following steps:

(a) attaching a first amino acid to a solid support

(b) condensing a second amino acid with the first,

(c) forming the DKP from the resulting dipeptide

Also stated (page 2371, second paragraph) is that Asp(OtBu) was used in the second coupling step, and the result was compound 4 (also depicted on page 2371). Variable "R" (compound 4) is not specifically identified, but it would be clear to a peptide chemist that "R" is intended to be the side chain of an amino acid.

Thus the claims are rendered obvious.

*

- Application 09/922234 was stricken from the IDS. Instead, USP 6,555,543 is now cited on the PTO-892.

- The following reference was stricken from the IDS because it was not received:

  Shimazaki (*J Med Chem* 30, 1709-11, 1987)

However, the following reference was received:

Shimazaki (*J Med Chem* 30, 1706-1709, 1987)

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at 571-272-0951. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

D. Lukton

DAVID LUKTON
PATENT EXAMINER
GROUP 1653